

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Application of: SENANAYAKE *et al.*

Application No.: To be assigned (Division of  
U.S. Application No. 10/160,033, filed 6/4/02)

Group Art Unit: To be assigned

Filed: Herewith

Examiner: To be assigned

For: METHODS OF TREATING OR  
PREVENTING PAIN USING  
SIBUTRAMINE METABOLITES  
(As amended)

Attorney Docket No.: 4821-535-999

**INFORMATION DISCLOSURE STATEMENT**

**Mail Stop Patent Application**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Pursuant to Applicants' duty of disclosure under 37 C.F.R. § 1.56, enclosed is a list of one hundred forty one (141) references for the Examiner's review and consideration. These references are listed on the enclosed Form PTO-1449 entitled "List of References Cited by Applicant." These references (AA-FK) are listed in reverse-chronological or alphabetical order. Copies of these references are not enclosed as the copies were submitted in connection with U.S. Application Nos. 10/160,033, 09/409,889 and 09/372,158, which are the parent and grandparents of this application. Copies will be provided, however, upon the Examiner's request.

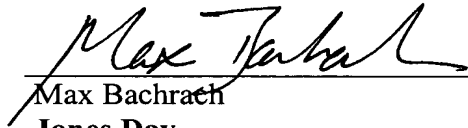
Identification of the foregoing references is not to be construed as an admission of Applicants or Attorneys for Applicants that such references are available as "prior art" against the subject application. Consequently, Applicants respectfully decline to use form PTO-1449, since that form identifies all of the references cited therein as "Prior Art." As an alternative, Applicants submit herewith a "revised form PTO 1449" entitled "List of References Cited."

Applicants respectfully request that the Examiner review the references and make them of record by completing and returning the enclosed List of References.

No fee is believed to be due for the submission of this statement as this statement is submitted prior to first office action on the merits. If any fees are required, however, please charge the required fees to Jones Day Deposit Account No. 503013.

Respectfully submitted,

Date March 23, 2004

  
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Enclosure

<b>LIST OF REFERENCES CITED BY APPLICANT</b> <i>(Use several sheets if necessary)</i>				ATTY. DOCKET NO 4821-535-999		APPLICATION NO To be assigned	
				APPLICANT SENANAYAKE <i>et al.</i>			
				FILING DATE Herewith		GROUP To be assigned	
<b>U.S. PATENT DOCUMENTS</b>							
*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	AA	6,174,925	01/2001	Bailey et al.			
	AB	6,127,363	10/2000	Doherty et al.			
	AC	6,046,242	11/1998	Emmelmann			
	AD	5,795,880	08/1998	Svec et al.			
	AE	5,780,051	07/1998	Eswara et al.			
	AF	5,733,566	03/1998	Lewis			
	AG	5,719,283	02/1998	Bell et al.			
	AH	5,674,553	10/1997	Shinoda et al.			
	AI	5,639,476	06/1997	Oshlack et al.			
	AJ	5,591,767	01/1997	Mohr et al.			
	AK	5,552,429	09/1996	Wong et al.			
	AL	5,459,164	10/1995	Vargas			
	AM	5,436,272	07/1995	Scheinbaum			
	AN	5,354,556	10/1994	Sparks et al.			
	AO	5,250,534	10/1993	Bell et al.			
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	AR	5,073,543	12/1991	Marshall et al.			
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	BA	4,814,352	03/1989	Jeffery et al.			
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	BD	4,552,828	11/1985	Toya et al.			
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	BN	3,155,669	11/1964	Janssen et al.			

### FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO
	BO	WO 00/56322	09/2000	PCT				
	BP	WO 00/56321	09/2000	PCT				
	BQ	WO 00/56320	9/28/2000	PCT				
	BR	WO 00/56318	09/2000	PCT				
	BS	WO 00/56315	09/2000	PCT				
	BT	WO 00/56314	09/2000	PCT				
	BU	WO 00/56309	09/2000	PCT				
	BV	WO 00/56306	09/2000	PCT				
	BW	WO 00/56151	09/2000	PCT				
	BX	WO 00/56150	09/2000	PCT				
	BY	WO 00/56149	09/2000	PCT				
	BZ	WO 00/56148	09/2000	PCT				
	CA	WO 00/54765	09/2000	PCT				
	CB	WO 00/32182	06/2000	PCT				
	CC	WO 00/10551	03/2000	PCT				
	CD	WO 99/33450	07/1999	PCT				
	CE	WO 98/13034	04/1998	PCT				
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	CJ	WO 97/20810	06/1997	PCT				
	CK	WO 97/03675	02/1997	PCT				
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	CN	WO 94/28902	12/1994	PCT				
	CO	WO 94/00114	01/1994	PCT				
	CP	WO 94/00047	01/1994	PCT				
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	CU	EP 0 035 597	9/1981	Europe				
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	CW	Buckett et al., "BTS 54 524-An Approach to Rapidly Acting antidepressant," <i>New Concepts in Depression</i> 2: 167-172 (1988).
	CX	Bucket et al., "The Pharmacology of Sibutramine Hydrochloride (BTS 54 524), A New Antidepressant which induces Rapid Noradrenergic Down-Regulation", <i>Prog. Neuro-Psychopharmacol. &amp; Biol. Psychiat.</i> 12: 575-584 (1988).
	CY	Buckett et al., "Sibutramine Hydrochloride," <i>Drugs of the Future</i> 13(8): 736-738 (1988).

CZ	Butler, D., <i>Facile Cycloalkylation of Arylacetonitriles in Dimethyl Sulfoxide</i> , J. Org. Chem., 36:1308-1309 (1971)
DA	Carstensen, J., <i>Drug Stability: Principles &amp; Practice</i> , 2d. Ed., pp. 379-80, Marcel Dekker, NY, NY, (1995).
DB	Castello, R.A., et al., <i>Discoloration of Tablets Containing Amines and Lactose</i> , Pharm. Sci. 51(2):106-108 (1962)
DC	Cheetham, S.C., et al., [ <sup>3</sup> H]Paroxetine Binding in Rat Frontal Cortex Strongly Correlates with [ <sup>3</sup> H]5-HT Uptake: Effect of Administration of Various Antidepressant Treatments, Neuropharmacology (1993), 32(8), 737-743
DD	<i>Diagnostic and Statistical Manual of Mental Disorders</i> , Fourth Ed., American Psychiatric Association, (1997).
DE	<i>Diagnostic and Statistical Manual of Mental Disorders</i> , 3rd Ed., American Psychiatric Association (1981).
DF	Dreshfield et al., <i>Enhancement of Fluoxetine-Dependent Increase of Extracellular Serotonin (5-HT) Levels by (-)-Pindolol, an Antagonist at 5-HT<sub>1A</sub> Receptors</i> , Neurochem. Res., 21(5):557-562 (1996)
DG	Eliel, E.L., <i>Stereochemistry of Carbon Compounds</i> (McGraw-Hill, NY, 1962).
DH	Evans et al., "Prevalence of Alzheimer's Disease in a Community Population of Older Persons," J.A.M.A. 262: 2551-2556 (1989).
DI	Fuentes, J. et al., "Comparison of the apparent anti-depressant activity of (-) and (+) tranylpromine in an animal model", <i>Chemical Abstracts</i> , 85: 7, page 31, No. 40768t (1976).
DJ	Goodman & Gilman, <i>The Pharmacological Basis of Therapeutics</i> , 362-373, 404 (9 <sup>th</sup> ed. McGraw-Hill, 1996)
DK	Gray et al., <i>The Involvement of the Opioidergic System in the Antinociceptive Mechanism of Action of Antidepressant Compounds</i> , BR.J. Pharmacol., Vol. 124, No. 4, (1998) pp 669-674
DL	<i>Handbook of Pharmaceutical Excipients</i> , 2 <sup>nd</sup> ed., Wade and Willer eds., pp. 257-259 (1994)
DM	Heal et al., <i>A Comparison of the Effects on Central 5-HT Function of Sibutramine Hydrochloride and Other Weight-Modifying Agents</i> , BR.J. Pharmacol. (1998), 125(2), 301-308
DN	J. Med. Chem., Vol. 36, No. 17, 2540 (1993)
DO	<i>Introduction to Pharmaceutical Dosage Forms</i> , 4th ed., Lea & Febiger, Philadelphia (1985).
DP	Jamali et al., <i>Journal of Pharmaceutical Sciences</i> , 78: 9: 695-715 (1989)
DQ	Jeffery et al., <i>Synthesis of Sibutramine, A Novel Cyclobutylalkylamine Useful in the Treatment of Obesity, and its Major Human Metabolites</i> , J. Chem. Soc. Perkin. Trans. 1, 2583-2589 (1996)
DR	King et al., "Clinical Pharmacology of Sibutramine Hydrochloride (BTS 54524) A New Antidepressant, in Healthy Volunteers," <i>Clinical Pharmac.</i> 26: 607-611 (1989).
DS	Kula et al., "Effects of N-Substituted Phenyltetrahydropyridines on Cerebral High-Affinity Synaptosomal Uptake of Dopamine and Other Monoamines in Several Mammalian Species," <i>Life Sciences</i> 34(26): 2567-2575, (1984).
DT	Luscombe et al., <i>The Contribution of Metabolites to the Rapid and Potent Down-Regulation of Rat Cortical <math>\beta</math>-Adrenoceptors by the Putative Antidepressant Sibutramine Hydrochloride</i> , Neuropharmacology, Vol. 28, No. 2, (1989) pp 129-134
DU	<i>The Merck Manual of Diagnosis and Therapy</i> , ??th Ed., Merck & Co., Inc., Whitehouse Station, NJ, (1999).
DV	Middlemiss et al., <i>Centrally Active 5-HT Receptor Agonists and Antagonists</i> , Neurosci. and Biobehv. Rev., 16:75-82 (1992)
DW	Moreau et al., <i>Behavioral Profile of the 5-HT<sub>1A</sub> Receptor Antagonist (S)-UH-301 in Rodents and Monkeys</i> , Brain Res. Bull., 29:901-04 (1992)
DX	Nakada et al., <i>An Enantioconvergent Route to (-)-Kainic Acid</i> , Tetrahedron Lett., 38:857-860 (1997)
DY	<i>Physician's Desk Reference</i> ® 473-475 (53 <sup>rd</sup> ed., 1999)
DZ	<i>Physician's Desk Reference</i> ® 475-476 (53 <sup>rd</sup> ed., 1999)
EA	<i>Physician's Desk Reference</i> ® 764-766 (53 <sup>rd</sup> ed., 1999)
EB	<i>Physician's Desk Reference</i> ® 823-825 (53 <sup>rd</sup> ed., 1999)
EC	<i>Physician's Desk Reference</i> ® 978-979 (53 <sup>rd</sup> ed., 1999)
ED	<i>Physician's Desk Reference</i> ® 1054-1056 (53 <sup>rd</sup> ed., 1999)
EE	<i>Physician's Desk Reference</i> ® 1332-1334 (53 <sup>rd</sup> ed., 1999)
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EG	<i>Physician's Desk Reference</i> ® 1432-1436 (53 <sup>rd</sup> ed., 1999)
EH	<i>Physician's Desk Reference</i> ® 1494-1498 (53 <sup>rd</sup> ed., 1999)
EI	<i>Physician's Desk Reference</i> ® 1641-1645 (53 <sup>rd</sup> ed., 1999)

EJ	<i>Physician's Desk Reference</i> ® 2004-2009 (53 <sup>rd</sup> ed., 1999)
EK	<i>Physician's Desk Reference</i> ® 2075-2078 (53 <sup>rd</sup> ed., 1999)
EL	<i>Physician's Desk Reference</i> ® 2190-2192 (53 <sup>rd</sup> ed., 1999)
EM	<i>Physician's Desk Reference</i> ® 2367-2368 (53 <sup>rd</sup> ed., 1999)
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EO	<i>Physician's Desk Reference</i> ® 2490-2493 (53 <sup>rd</sup> ed., 1999)
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EQ	<i>Physician's Desk Reference</i> ® 2688-2691 (53 <sup>rd</sup> ed., 1999)
ER	<i>Physician's Desk Reference</i> ® 2701-2704 (53 <sup>rd</sup> ed., 1999)
ES	<i>Physician's Desk Reference</i> ® 2720-2726 (53 <sup>rd</sup> ed., 1999)
ET	<i>Physician's Desk Reference</i> ® 2735-2736 (53 <sup>rd</sup> ed., 1999)
EU	<i>Physician's Desk Reference</i> ® 2886-2888 (53 <sup>rd</sup> ed., 1999)
EV	<i>Physician's Desk Reference</i> ® 2908-2910 (53 <sup>rd</sup> ed., 1999)
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EY	<i>Physician's Desk Reference</i> ® 3224-3225 (53 <sup>rd</sup> ed., 1999)
EZ	<i>Physician's Desk Reference</i> ® 3267-3272 (53 <sup>rd</sup> ed., 1999)
FA	<i>Physician's Desk Reference</i> ® 3307-3309 (53 <sup>rd</sup> ed., 1999)
FB	<i>Physician's Desk Reference</i> ® 3383-3384 (53 <sup>rd</sup> ed., 1999)
FC	<i>Physician's Desk Reference</i> ® 2520 (52 <sup>nd</sup> ed., 1998)
FD	<i>Physician's Desk Reference</i> ® 2958 (52 <sup>nd</sup> ed., 1998)
FE	<i>Remington's: The Practice of The Science and Pharmacy</i> , 19 <sup>th</sup> ed., Gennaro, ed., p. 1625 (1995)
FF	<i>Remington's Pharmaceutical Sciences</i> , 18th ed., Mack Publishing, Easton PA (1990).
FG	<i>Remington's Pharmaceutical Sciences</i> , 16th ed., Mack Publishing, Easton PA (1980).
FH	Stock, M.J., <i>Sibutramine: A Review of the Pharmacology of a Novel Anti-Obesity Agent</i> , Int'l J. Obesity, 21(Supp. 1):S25-S29 (1997)
FI	U.S. Pharmacopia (USP) SP (XXI)/NF (XVI)
FJ	Wilen et al., <i>Tetrahedron</i> , 2725-36 33(21) (1977).
FK	Wilen, S.H., <i>Tables of Resolving Agents and Optical Resolutions</i> 268 (E.L. Eliel ed., Univ. of Notre Dame Press, Notre Dame, IN, 1972).

**EXAMINER**

**DATE CONSIDERED**

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.